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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/088,868 | 06/24/2002 | Jana Lenz | 3868-0112P | 6750 |

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| EXAMINER | |
|---|---|
| PADMANABHAN, KARTIC | |
| **ART UNIT** | **PAPER NUMBER** |
| 1641 | |

DATE MAILED: 10/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/088,868 | LENZ ET AL. | |
| | Examiner | Art Unit | |
| | Kartic Padmanabhan | 1641 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *19 August 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Priority*

1. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

### *Specification*

#### Content of Specification

(a) Title of the Invention: See 37 CFR 1.72(a) and MPEP § 606. The title of the invention should be placed at the top of the first page of the specification unless the title is provided in an application data sheet. The title of the invention should be brief but technically accurate and descriptive, preferably from two to seven words may not contain more than 500 characters.

(b) Cross-References to Related Applications: See 37 CFR 1.78 and MPEP § 201.11.

(c) Statement Regarding Federally Sponsored Research and Development: See MPEP § 310.

(d) Incorporation-By-Reference Of Material Submitted On a Compact Disc: The specification is required to include an incorporation-by-reference of electronic documents that are to become part of the permanent United States Patent and Trademark Office records in the file of a patent application. See 37 CFR 1.52(e) and MPEP § 608.05. Computer program listings (37 CFR 1.96(c)), "Sequence Listings" (37 CFR 1.821(c)), and tables having more than 50 pages of text were permitted as electronic documents on compact discs beginning on September 8, 2000.

Or alternatively, Reference to a "Microfiche Appendix": See MPEP § 608.05(a). "Microfiche Appendices" were accepted by the Office until March 1, 2001.

(e) Background of the Invention: See MPEP § 608.01(c). The specification should set forth the Background of the Invention in two parts:

(1) Field of the Invention: A statement of the field of art to which the invention pertains. This statement may include a paraphrasing of the applicable U.S. patent classification definitions of the subject matter of the claimed invention. This item may also be titled "Technical Field."

(2) Description of the Related Art including information disclosed under 37 CFR 1.97 and 37 CFR 1.98: A description of the related art known to the applicant and including, if applicable, references to specific related art and problems involved in the prior art which are solved by the applicant's invention. This item may also be titled "Background Art."

(f) Brief Summary of the Invention: See MPEP § 608.01(d). A brief summary or general statement of the invention as set forth in 37 CFR 1.73. The summary is separate and distinct from the abstract and is directed toward the invention rather than the disclosure as a whole. The summary may point out the advantages of the invention or how it solves problems previously existent in the prior art (and preferably indicated in the Background of the Invention). In chemical cases it should point out in general terms the utility of the invention. If possible, the nature and gist of the invention or the inventive concept should be set forth. Objects of the invention should be treated briefly and only to the extent that they contribute to an understanding of the invention.

(g) Brief Description of the Several Views of the Drawing(s): See MPEP § 608.01(f). A reference to and brief description of the drawing(s) as set forth in 37 CFR 1.74.

(h) Detailed Description of the Invention: See MPEP § 608.01(g). A description of the preferred embodiment(s) of the invention as required in 37 CFR 1.71. The description should be as short and specific as is necessary to describe the invention adequately and accurately. Where elements or groups of elements, compounds, and processes, which are conventional and generally widely known in the field of the invention described and their exact nature or type is not necessary for an understanding and use of the invention by a person skilled in the art, they should not be described in detail. However, where particularly complicated subject matter is involved or where the elements, compounds, or processes may not be commonly or widely known in the field, the specification should refer to another patent or readily available publication which adequately describes the subject matter.

(i) Claim or Claims: See 37 CFR 1.75 and MPEP § 608.01(m). The claim or claims must commence on separate sheet or electronic page (37 CFR 1.52(b)(3)). Where a claim sets forth a plurality of elements or steps, each element or step of the claim should be separated by a line indentation. There may be plural indentations to further segregate subcombinations or related steps. See 37 CFR 1.75 and MPEP § 608.01(i)-(p).

(j) Abstract of the Disclosure: See MPEP § 608.01(f). A brief narrative of the disclosure as a whole in a single paragraph of 150 words or less commencing on a separate sheet following the claims. In an international application which has entered the national stage (37 CFR 1.491(b)), the applicant need not submit an abstract commencing on a separate sheet if an abstract was published with the

international application under PCT Article 21. The abstract that appears on the cover page of the pamphlet published by the International Bureau (IB) of the World Intellectual Property Organization (WIPO) is the abstract that will be used by the USPTO. See MPEP § 1893.03(e).

(k) Sequence Listing, See 37 CFR 1.821-1.825 and MPEP §§ 2421-2431. The requirement for a sequence listing applies to all sequences disclosed in a given application, whether the sequences are claimed or not. See MPEP § 2421.02.

***Applicant should include headings for the pertinent sections of the specification, as outlined above.***

2. The disclosure is objected to because of the following informalities: the specification contains Tables 1 and Tables 3-7, but there does not appear to be a Table 2.

Appropriate correction is required.

***Claim Rejections - 35 USC § 112***

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5. Claim 1 is rejected as vague and indefinite for the recitation of "possibly liberating and isolating" in step d) because it is unclear if liberation and isolation are required steps of the claim or not. In addition, applicant should insert "A" at the beginning of the claim so it reads "A process."

6. In claims 2-20, applicant should change "Process" at the beginning of the claim to "The Process."

7. Claim 4 recites the limitations "the pH value" and "the aqueous solution" in line 2 of the claim. There is insufficient antecedent basis for these limitations in the claim.

8. Claim 4 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite in that it fails to point out what is included or excluded by the claim language. This claim is an omnibus type claim. The recitation of a "suitable buffer" does not allow one to adequately determine the metes and bounds of the claim.

9. Claim 8 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite in that it fails to point out what is included or excluded by the claim language. This claim is an omnibus type claim. The recitation of "other suitable methods" does not allow one to adequately determine the metes and bounds of the claim.

10. Regarding claim 9, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

11. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd.

App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 9 recites the broad recitation LC-MS or MS-MS, and the claim also recites microcapillary or nano-HPLC, which is the narrower statement of the range/limitation.

12. Regarding claim 10, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

13. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 10 recites the broad recitation LC-MS or MS-MS, and the claim also recites microcapillary or nano-HPLC, which is the narrower statement of the range/limitation.

14. Claim 18 recites the limitation "the enzyme thrombin." There is insufficient antecedent basis for this limitation in the claim.

15. Claim 19 recites the limitation "the receptor trypsin." There is insufficient antecedent basis for this limitation in the claim.

16. Claim 20 recites the limitation "the $\beta_2$-adrenoreceptor." There is insufficient antecedent basis for this limitation in the claim.

17. Claim 21 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are all the elements of the device. In a claim drawn to a device, all the elements required for the proper functioning of the device must be positively recited in the claim.

***Claim Rejections - 35 USC § 102***

18. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

19. Claims 1-17 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Zuckermann et al. (Proc. Natl. Acad. Sci., 1992). The reference discloses the screening of a library of 361 peptides. The library was synthesizes as 19 pools of 19 peptides. Each pool was screened in a solution phase competition ELISA assay. The 12 most inhibitory peptides were isolated by rapid-affinity selection and were identified by mass spectrometry and amino acid analysis (abstract). Peptides were also characterized using HPLC (p. 4505, 2nd column). In performing the ELISA of the peptide pools, microtiter plates were coated with recombinant antigen, and an aliquot of the peptide pool was incubated with IgG in a phosphate buffer. The

plates were washed and incubated with horseradish peroxidase. The plates were washed again and bound conjugated antibody was quantified by color development. Each of the four most inhibitory pools was affinity-selected with monoclonal antibody. The IgG-peptide complex was separated from excess free peptide by gel-filtration chromatography. The bound peptides were further analyzed by reverse phase HPLC, and peaks were identified by mass spectrometry.

20. Claims 1-12, 16-17, and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by van Breemen et al. (Anal. Chem., 1997). The reference discloses a pulsed ultrafiltration mass spectrometry method for screening combinatorial libraries. The method allows for the identification of solution-phase ligands in library mixtures that bind to solution-phase receptors. After ligands contained in the library were bound to a receptor, the complexes were purified by ultrafiltration and then dissociated with methanol to elute the ligands into the electrospray mass spectrometer for detection (abstract). A library of 19 adenosine analogs plus adenosine, the natural substrate for adenosine deaminase, was prepared in potassium phosphate buffer. After injecting the mixture into the ultrafiltration chamber, the chamber was flushed with water to remove unbound compounds. The enzyme ligand complex was then dissociated and ligands were analyzed by electrospray mass spectrometry (page 2160).

21. Claims 1-12, 16-17, and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Wieboldt et al. (Anal. Chem., 1997). The reference discloses immunoaffinity ultrafiltration with ion spray HPLC/MS for screening small-molecule libraries. The solution phase screening method of the reference is applicable to screening combinatorial libraries of 20-30 closely related molecules. Individual benzodiazepines are selected from a multicomponent library mixture by formation in solution of non-covalent immunoaffinity complexes with antibodies. Captured

compounds are then separated from non-specifically bound library components by centrifugal ultrafiltration. The molecules retained on the filter are liberated from the antibodies and analyzed by HPLC coupled with electrospray mass spectrometry (page 1683). The pooled mixtures of benzodiazepines were prepared in ammonium acetate buffer.

***Claim Rejections - 35 USC § 103***

22. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

23. The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

24. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

25. Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Zuckermann et al. (Proc. Natl. Acad. Sci., 1992), van Breemen et al. (Anal. Chem. 1997) or Wieboldt et al. (Anal. Chem., 1997) in view of Kunihiro et al. (US Pat. 5,300,490).

Zuckermann et al., van Breemen et al., and Wieboldt et al. teach processes for identifying a substance in a mixture, as previously discussed under 35 USC 102. However, none of the references teach the use of thrombin.

Kunihiro et al. teach the use of thrombin as the ligand on an affinity resin to bind analyte.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to use thrombin as taught by Kunihiro et al. with the methods of Zuckermann et al., van Breemen et al. or Wieboldt et al. because Kunihiro et al. teach the use of thrombin as a receptor in ligand binding assays, such as purification. In addition, thrombin is commonly used in ultrafiltration to bind a substance before being removed for analysis of the substance, and depending on the molecule of interest, one would have known the appropriate target to use. Furthermore, it has been held to be within the general skill of a worker in the art to select a known material on the basis of its suitability for the intended use as a matter of obvious design choice. *In re Leshin*, 125 USPQ 416.

26. Claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over Zuckermann et al. (Proc. Natl. Acad. Sci., 1992), van Breemen et al. (Anal. Chem. 1997) or Wieboldt et al. (Anal. Chem., 1997) in view of Kurome et al. (US Pat. 5,824,503).

Zuckermann et al., van Breemen et al., and Wieboldt et al. teach processes for identifying a substance in a mixture, as previously discussed under 35 USC 102. However, none of the references teach the use of trypsin.

Kurome et al. teach the use of trypsin to bind and digest various molecules.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to use thrombin as taught by Kurome et al. with the methods of Zuckermann et al., van Breemen et al. or Wieboldt et al. because thrombin is commonly used in binding/isolation assays, and depending on the molecule of interest, one would have known the appropriate target to use. Furthermore, it has been held to be within the general skill of a worker in the art to select a known material on the basis of its suitability for the intended use as a matter of obvious design choice. *In re Leshin*, 125 USPQ 416.

27. Claim 20 is rejected under 35 U.S.C. 103(a) as being unpatentable over Zuckermann et al. (Proc. Natl. Acad. Sci., 1992), van Breemen et al. (Anal. Chem. 1997) or Wieboldt et al. (Anal. Chem., 1997) in view of Soppet et al. (US Pat. 6,338,951).

Zuckermann et al., van Breemen et al., and Wieboldt et al. teach processes for identifying a substance in a mixture, as previously discussed under 35 USC 102. However, none of the references teach the use of $ß_2$ adrenoreceptor.

Soppet et al. teach methods for the screening of compounds which bind to G-protein coupled receptors, such as $ß_2$ adrenoreceptor.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to use $ß_2$ adrenoreceptor as taught by Soppet et al. with the methods of Zuckermann et al., van Breemen et al. or Wieboldt et al. because Soppet et al. teach the use of G-protein coupled receptors in screening assays. In addition, depending on the molecule of interest, one would have known the appropriate target to use. Furthermore, it has been held to be within the general skill of a worker in the art to select a known material on the basis of its

suitability for the intended use as a matter of obvious design choice. *In re Leshin*, 125 USPQ 416.

***Conclusion***

Claims 1-21 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kartic Padmanabhan whose telephone number is 571-272-0825. The examiner can normally be reached on M-F (8:30-5:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Kartic Padmanabhan
Patent Examiner
Art Unit 1641

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Christopher L. Chin

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PRIMARY EXAMINER
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